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Attorney's Docket No.: 16596-018001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Matthew C. Coffey, et al. Art Unit : 1642
Serial No. : 10/076,074 Examiner : Sheela J. Huff
Filed : February 15, 2002
Title : SENSITIZATION OF CHEMOTHERAPEUTIC AGENT RESISTANT NEOPLASTIC CELLS WITH A VIRUS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. § 1.56, Applicants hereby submit the following information in conformance with 37 C.F.R. §§ 1.97 and 1.98. Pursuant to C.F.R. § 1.98, a copy of each newly cited document is enclosed.

Applicants submit the following reference listed on the attached form PTO-1449.

1. HIRASAWA, K. et al., Reovirus Therapy of Metastatic Cancer Models in Immune-competent Mice, on the web site of Oncolytics Biotech, Inc. (http://www.oncolyticsbiotech.com/022801p1.html) (2001).

Applicants would like to take this opportunity to submit a correction for a typographical error discovered in Applicant's most recent information disclosure statement and form PTO-1449. Namely, an incorrect page number was listed for the following citation (shown corrected): Fujiwara et al., Induction of Chemosensitivity in Human Lung Cancer Cells *in Vivo* by Adenovirus-mediated Transfer of the Wild-type *p53* Gene, *Cancer Research* **54**:2287-2291 (1994). A copy of said citation wherein the true and correct page numbers appear has previously been submitted.

This statement is being filed before a first Office Action on the merits, therefore no fee is required under 37 C.F.R. § 1.97(b). In the event an Office Action is mailed by the United States

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April 1, 2004
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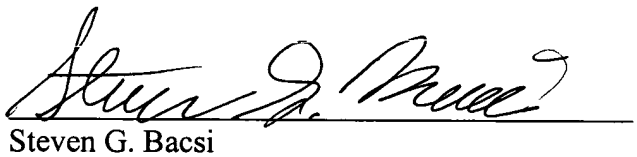
Patent and Trademark Office prior to receipt of this Supplemental Information Disclosure Statement, Applicants hereby make the statement as specified in 37 C.F.R. § 1.97(e) that the document contained herein was first cited in a communication from a foreign patent office in a counterpart foreign application within three months of the filing of this Supplemental Information Disclosure Statement. Therefore, no fee is required under 37 C.F.R. §1.97(c).

To assist the Examiner, the document is listed on the attached form PTO-1449. It is respectfully requested that an Examiner initialed copy of this form be returned to the undersigned.

Should it be determined that a fee is due, please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 4-1-04



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| Substitute Form PTO-1449 (Modified) | U.S. Department of Commerce Patent and Trademark Office | Attorney's Docket No. 16596-018001 | Application No. 10/076,074 |
|---|---|---|---|
| **Information Disclosure Statement by Applicant** (Use several sheets if necessary) (37 CFR §1.98(b)) | | Applicant Matthew C. Coffey, et al. | |
| | | Filing Date February 15, 2002 | Group Art Unit 1642 |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
|---|---|---|---|---|---|---|---|
| | AA | | | | | | |
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| | AP | | | | | | | |

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document |
|---|---|---|
| | AQ* | HIRASAWA, K. et al., Reovirus Therapy of Metastatic Cancer Models in Immune-competent Mice, on the web site of Oncolytics Biotech, Inc. (http://www.oncolyticsbiotech.com/022801p1.html) (2001). |
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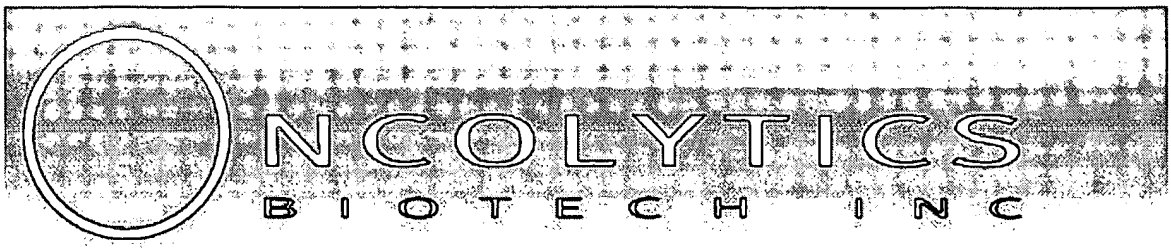
EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.






## Technology & Product

### REOVIRUS THERAPY OF METASTATIC CANCER MODELS IN IMMUNE-COMPETENT MICE

*Kensuke Hirasawa, Chang-Soon Yoon, Sandra G. Nishikawa, David M. Waisman, Patrick WK Lee, University of Calgary, Calgary, AB, Canada.*

Reovirus selectively replicates in and destroys cancer cells with an activated Ras signaling pathway. We have previously reported that direct intratumoural injection of reovirus resulted in tumour regression in mice. The application of reovirus therapy to metastatic cancer models would be the next challenge. The objective of this study is to examine the effects of intravenous (i.v.) reovirus treatment in metastatic models of immune-competent mice. First, the maximum tolerated i.v. dose of reovirus in C3H mice was determined to be 5X10(8) plaque forming units (PFU)/mouse. Using immune-competent C3H mice implanted with ras-transformed C3H-10T1/2 cells (C3 cells) at the hind flank, i.v. administration of reovirus (4 times 5X10(8) PFU's) resulted in significant reduction of tumour volumes. Combined treatment of reovirus with cyclosporine A (50 mg/kg) or cisplatin (3.0 mg/kg) further reduced the tumour size. To determine if reovirus therapy could be applied to experimental metastasis animal models, C3-L5 cells were introduced intravenously into C3H mice, which induced rapid metastasis in the lung. Subsequent i.v. treatment with reovirus (4 times 5X10(8) PFU's) resulted in significant enhancement of survival rate of these animals. We also examined the effect of i.v. reovirus therapy in the Lewis lung carcinoma metastasis mouse model, in which removal of the primary tumour invariably leads to rapid metastasis in the lung. We found that i.v reovirus treatment resulted in significant reduction in tumour burden in these animals (based on the number of lung metastatic foci and lung weight). In conclusion, i.v. treatment of reovirus is effective in metastastic cancer models of immune-competent animals.



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